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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,615	11/13/2000	Kenneth F. Buechler	230/006	4653

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EXAMINER	
COOK, LISA V	
ART UNIT	PAPER NUMBER
1641	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/712,615	BUECHLER ET AL.	
	Examiner	Art Unit	
	LISA V. COOK	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27,28 and 93-128* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *97,98,105,106,119 and 120* is/are allowed.

6)☒ Claim(s) *27,28, 93-96, 99-104, 107-118,and 121-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. Applicants response to the Action mailed 10/18/07 is acknowledged (paper filed 11/29/07). In the response filed therein claims 1-26 and 29-92 were canceled. Claims 97, 105, and 119 were modified. Currently claims 27, 28, and 93-128 are pending and under consideration.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 102/103

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

I. Claims 27, 93, 94, 96, 99-100, 109-116, 118, and 121-126 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Buechler (U.S. Patent #5,458,852).

Buechler discloses assay devices meeting the requirements of the instant invention. This is supported by the specification on page 59, lines 21-28. Particularly Buechler's device comprises a reaction chamber (column 6) and a diagnostic lane (column 10 –diagnostic element). See figures 1-5, item #4 (reaction chamber, column 6 and 7), item #17 (optional reagent chambers, column 8 and 9, and item # 6 (diagnostic element, column 10).

The device includes a time gate for measuring the reaction in a given period of time. Please see column 7 lines 41-45. The device is useful in measuring an absolute signal or a rate of change of the signal.

Particularly determining the presence or amount of each target ligand in the sample either visually or instrumentally, column 17, lines 44-46. The rate of change is monitored via the flow rate of reagents through the porous member, column 18, lines 2-9. Further the label (signal development element) does not appreciably bind to any reagent in said assay device but could be designed to indirectly cause a visually or instrumentally detectable signal because of the assay process, column 3, lines 17-25.

The apparatus of Buechler further includes an optical system for detecting and processing optical signals generated from the label in the diagnostic lane. Column 20 lines 22-31.

As illustrated in Figure 1, Buechler discloses "diagnostic testing devices for determining the presence or amount of at least one target ligand' which comprise "various elements, [including] a sample addition zone **1**, a sample addition reservoir **2**, a sample reaction barrier **3**, a reaction chamber **4**, a time gate **5**, a diagnostic element **6**, and a used reagent reservoir **7**" (Buechler, Fig.1 and col. 4, 1. 63, to col. 5, 1, 3).

The diagnostic element contains one or more capture zones, and "various means can be used for the detection of signal at the capture zone of the diagnostic element….[including] visual and instrumental means, such as spectrophotomeric and reflectance [means]" (id. At col. 11, II. 21-31). Focusing on Buechler's "time gate,", Buechler teaches that "the time gate **5** holds the reaction mixture in the reaction chamber **4** for a given period of time.., relative to the assay process such that the reactions which occurs in the reaction chamber **4** as a result of the assay process will reflect the presence or amount of target ligand in the sample. Thus, the time gate **5** delays the flow of the reaction mixture onto the diagnostic element **6**" (Buechler, Fig. 1A, col. 7, 11.41-53).

Buechler, in discussing the diagnostic element, and referring to Figures 1 and 2, teaches that "capture zones are comprised of reagents, such as receptors….which bind or react with one or more components from the reaction mixture. The binding of the reagents from the reaction mixture to the capture zones of the diagnostic element 6 is related to the presence or amount of target ligand in the sample" (Buechler, col. 10, 11. 10-19). These "capture zones" appear to be the same as the claimed "assay zones" because they are configured to bind analyte, the same function the "assay zones" are required to have by the claim. Moreover, Buechler's receptors "can be placed in discrete zones" (*id* at col. 10, 11. 21-23). In addition to the reagents that bind or react with the target ligand, Buechler teaches that "[r]eceptors or other chemical reagents, for example, a receptor against the signal generator can also be immobilized on the diagnostic element **6** to verify to the user that the reagents of the reaction mixture are viable and that the reaction mixture passed through the zones of the receptors or biosensors" (*id*. at col. 10, 11. 24-29).

Buechler describes a positive control analogous to the independent assay control described in the present specification. See Buechler, col. 14, II. 25-66. *"The reaction mixture may also flow over a positive control zone, which can be for example, an immobilized receptor to the signal development element……"* Buechler's positive control appears to be designed to independently confirm that the assay reagents have actually passed over the capture zones, i.e., that the assay has run to completion.

Since the signal-producing reagent used to detect the target in the capture zone(s) is the same signal-producing reagent that binds to the positive control, it is logical to assume that the capture zone(s) and the positive control zone are separate, discrete zones on the surface of the diagnostic element. Otherwise, the target and control signals would be indistinguishable. Moreover, it is logical to assume that Buechler's device is configured such that both the positive control zone and the capture zone can be accessed visually or instrumentally to determine whether the signal producing reagent has contact both zones. Consequently, the claimed optical component appears to be anticipated by the cited reference of Buechler.

In the alternative, Buechler differs from the instant invention in not specifically disclosing the detailed structure of the optical system including an optical component and a signal processor specifically configured to read electronic signals. In particular, while Buechler's "time gate" is in fluid communication with a reaction chamber and an assay zone, and in use, contains optically detectable labels, Buechler's optical component is not appropriately configured (Br.17) to detect a signal from the optically detectable label within the time gate.

However, even if the claimed assay device is not identical to the device of Buechler with regard to the configuration of the optical component to allow for detection in the "time gate", the differences is deemed obvious because one of ordinary skill in the art would have been motivated to measure the label reagents in the "time gate" in order to detect the reagents through out the device as a means of tracking reagent flow, assay progression, and assay completion. In other words, Buechler's device contains a positive control analogous to the independent control described in the present specification. The positive control appears to be designed to independently confirm that the assay reagents have actually passed over the capture zones, i.e., that the assay has run to completion. It would have been prima facie obvious to include an optical system in the device of Buechler such that the positive control and the capture zone can be accessed visually or instrumentally in order to determine the signal producing reagents within the device. This would allow for the detection of all the labeled reagents and their effects within the assay device. Absent evidence to the contrary the invention is alternatively considered obvious.

Response to Arguments

3. A. Anticipation rejection based on Buechler, US Patent #5,458,852

Applicant contends that the Examiner continues to analyze the '852 patent from a flawed perspective, because the "time gate" of the '852 patent is not involved in measuring any reaction. This argument was carefully considered but not found persuasive because Buechler discloses that the "time gate" is involved in the measurement of binding reactions. First, the "time gate" holds

the **reaction** mixture in the reaction chamber for a given period of time. See column 7 lines 41-42.

The amount of time for which the "time gate" holds the reaction mixture is related to the rate of binding (Applicants' rate of change) of a component(s) from the reaction mixture to the hydrophobic barrier. See column 8 lines 4-7. Second, the time delay provided by the "time gate" depends on the concentration of the component(s) in the reaction mixture. See column 8 lines 20-22, for example. Accordingly, it is reiterated that Buechler discloses a "time gate" for measuring the reaction in a given period of time.

Applicant further argues that the optical component in Buechler is not in the correct position to detect a signal from the optically detectable label within the time gate. This argument was carefully considered but not found persuasive because Buechler discloses the use of a biosensor to measure the presence or amount of target ligands. See column 3 lines 54-64. The biosensor or devices can be configured in discrete zones on the diagnostic element or they can be distributed homogeneously or heterogeneously over the surface. See column 10 lines 21-24. Buechler also teaches that the biosensor can be placed over the majority of the diagnostic element such that the **distance** which the component of the reaction mixture binds would be related to the concentration of the target ligand in the sample. See column 10 lines 29-37. In other words the optical signal which is measured and related to the analyte of interest may be generated in zones or over the majority of the element. The majority of the element would include the "time gate" and therefore it is deemed that Buechler anticipated the measurement of a biosensor in the "time gate" which relates to analyte flow or distance.

Applicant argues that the positive controls taught by the prior art are used to detect "false negatives" (determine if the reagents are still active or viable) instead of the time of assay completion. And this is the principle difference between the present invention and the prior art. This argument has been carefully considered but not found persuasive because Buechler teaches that the reagents can be immobilized on the diagnostic element to verify reagent viability and reagent flow (timing). See column 10 lines 24-29, for example. The measurement of reagent flow is taught by Buechler to be related to reaction time of completion and/or flow through the diagnostic element. Thus the reagents in the positive control are not only employed in reagent viability as argued by Applicant.

Applicant argues that the Buechler does not teach that the signal processor is configured to receive an electronic signal to determine the progress and time of completion of an assay for the analyte of interest from at least one of a rate of change of the amount of the electronic signal and an amount of the electronic signal as recited in the instant claims. This argument was carefully considered but not found persuasive because it has been held that a recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus satisfying the claimed structural limitations. *Ex parte Masham*, 2 USPQ2d 1647 (1987).

Accordingly the rejection is maintained.

B. Obviousness rejection based on Buechler, US Patent #5,458,852

Applicant argues that the optical component in Buechler is not in the correct position to detect a signal from the optically detectable label within the time gate. This argument was carefully considered but not found persuasive because Buechler discloses the use of a biosensor to measure the presence or amount of target ligands. See column 3 lines 54-64. The biosensor or devices can be configured in discrete zones on the diagnostic element or they can be distributed homogeneously or heterogeneously over the surface. See column 10 lines 21-24.

Buechler also teaches that the biosensor can be placed over the majority of the diagnostic element such that the **distance** which the component of the reaction mixture binds would be related to the concentration of the target ligand in the sample. See column 10 lines 29-37. In other words the optical signal which is measured and related to the analyte of interest may be generated in zones or over the majority of the element. The majority of the element would include the "time gate" and therefore it is deemed that Buechler makes the measurement of a biosensor in the "time gate" which relates to analyte flow or distance obvious.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 95 and 117 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Buechler (U.S. Patent #5,458,852) in view of Slovacek et al. (U.S. Patent#5,242,837).

Please see Buechler (U.S. patent #5,458,852) as set forth above.

The primary references do not particularly exemplify the use of a fluorometer as a useful optical detector.

However, fluorometers are routinely utilized to detect specific binding reagents. This point is supported in the patent of Slovacek et al. Therefor the use of a fluorometer is routine optimizations that are almost always determined and used in immunoassay studies.

Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to employ different known detectors in the given parameters to determine the unknown as a means of optimizing the device provided by the art.

III. Claims 28, 101, 102, 104, 107-108 and 127-128 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Buechler (U.S. Patent #5,458,852) in view of Foster et al. (U.S.Patent#4,444,879).

The teachings of Buechler (U.S. patent #5,458,852) as set forth above. However, these references fail to teach the assay as a kit.

However, kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a micro plate, positive controls, negative controls, standards, and instructions are taught. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay as taught by Buechler (U.S. patent #5,458,852) and format them into a kit because Foster et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminate the variability that can occur when performing the assay.

IV. Claim 103 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Buechler (U.S. Patent #5,458,852) in view of Foster et al. (U.S.Patent#4,444,879) as applied to claims 28, 101, 102, 104, 107-108 and 127-128 above, and further in view of Slovacek et al. (U.S. Patent#5,242,837).

Please see Buechler (U.S. patent #5,458,852) in view of Foster et al. as set forth above.

The primary references do not particularly exemplify the use of a fluorometer as a useful optical detector.

However, fluorometers are routinely utilized to detect specific binding reagents. This point is supported in the patent of Slovacek et al. Therefor the use of a fluorometer is routine optimizations that are almost always determined and used in immunoassay studies.

Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to employ different known detectors in the given parameters to determine the unknown as a means of optimizing the device provided by the art.

Response to Arguments

5. With respect to the additional rejections including Slovacek et al. (U.S. Patent#5,242,837) and Foster et al. (U.S.Patent#4,444,879), Applicant argues that primary '852 patents do not anticipate and/or make obvious the claimed invention and therefore cannot be combined to teach the other dependent claims. The arguments primary "852 patent has been addressed a priori and is maintained. therefore, the additional rejections are maintained.

Allowable Subject Matter

6. Claims 97, 98, 105, 106, 119, and 120 are allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action.

In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lisa V. Cook/

Examiner, Art Unit 1641

/Long V Le/

Supervisory Patent Examiner, Art Unit 1641